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10/511,362	10/15/2004	Perry J Blackshear	4239-64828-02	3754

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EXAMINER	
NGUYEN, QUANG	
ART UNIT	PAPER NUMBER
1633	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,362	BLACKSHEAR ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-21,25-31,33-41,43-46,49-59 and 61-73* is/are pending in the application.

4a) Of the above claim(s) *7,14,28-31,33-41,43-46,49-59 and 61-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-6, 8-13, 15-17, 19-21, 25-27 and 65-73* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 2/9/09 was entered.

Claims 5-21, 25-31, 33-41, 43-46, 49-59 and 61-73 are pending in the present application.

Applicant's election with traverse of SEQ ID NO:33 in the reply filed on 2/9/09 is acknowledged. The traversal is on the ground(s) that SEQ ID NO:33 and SEQ ID NO:34 are identical 14 amino acid sequences, while SEQ ID NO:35 differs from SEQ ID NOs:33 and 34 by one amino acid substitution at position 2. Therefore, it would not be undue burden on the examiner to search all of the above SEQ ID NOs.

Upon further consideration SEQ ID NO:33 and SEQ ID NO:34 will be examined together since they are identical. The examiner is not aware that the same sequence is identified by two different SEQ ID NOs. However, SEQ ID NO:35 will still be restricted from SEQ ID NO:33 and SEQ ID NO:34 because it is a different sequence and each different sequence or structure can be considered to be a "special technical feature". It would be undue burden for the examiner to search and consider all of these SEQ ID NOs in addition to numerous other elected SEQ ID NOs such as SEQ ID NO:8, SEQ ID NO:37, SEQ ID NO:11.

The requirement is still deemed proper and is therefore made FINAL.

Applicants also elected previously the following species: (a) SEQ ID NO:8 (corresponding SEQ ID NO:37) as a species of an encoded polypeptide; and (b) SEQ ID NO:11 as a species of a promoter.

Claims 7, 14, 28-31, 33-41, 43-46, 49-59 and 61-64 were withdrawn previously because they are directed to non-elected invention and non-elected species (claim 7).

This application contains claims 14, 28-31, 33-41, 43-46, 49-59 and 61-64 drawn to an invention nonelected without traverse in the reply filed on 11/01/07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Accordingly, amended claims 5-6, 8-13, 15-21, 25-27 and new claims 65-73 are examined on the merits herein with the above elected species.

Response to Amendment

The rejection under 35 USC 101 because the claimed invention is directed to non-statutory subject matter was withdrawn in light of Applicant's amendment with the new limitation "An in vitro host cell".

The rejection under 35 U.S.C. 102(e) as being anticipated by Nakayama et al. (WO 02/086071; IDS) was withdrawn in light of Applicant's amendment with the new limitation "a polynucleotide consisting of nucleotides 1-42".

The rejection under 35 U.S.C. 102(b) as being anticipated by Griffin et al. (Genes, Chromosomes & Cancer 4:153-157, 1992) as evidenced by Blackshear et al. (Development 130(19):4539-4552, 2003; IDS) was withdrawn in light of the definition of the term "isolated" of the present application.

Sequence Non-Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth below.

This application contains **two different nucleotide sequences listed in Fig. 1 which were not identified with proper SEQ ID NOs in either the Fig. 1 or in the Brief Description of the Figures; nor were these nucleotide sequences listed in either a sequence paper listing or in a computer readable form (CRF)**.

Note that failure to respond to this requirement will be considered non-compliant.

Claim Objections

Claim 25 is objected to because of the phrase "the N-terminus of the polypeptide is at least 90% identical to residues 1-14 of SEQ ID NO:8". This is because the N-terminus of a polypeptide is usually referring to a single N-terminal amino acid residue. Appropriate correction is required.

Claim 27 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. This is because claim 27 recites the limitation "the polynucleotide **comprising nucleotides 1-42** of SEQ ID

NO:37", and yet in claim 15 from which claim 27 is dependent on there is a limitation of "a polynucleotide **consisting of nucleotides 1-42 of**".

Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-6, 8-13, 25 and 65-71 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. ***This is a slightly modified rejection necessitated by Applicant's amendment.***

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

With respect to the elected invention and elected species (SEQ ID NO:37), the instant claims are drawn to an isolated nucleic acid molecule encoding a substantially

purified RFX4_v3 polypeptide, wherein the polypeptide comprises: a) an amino acid sequence **at least 70% identical (including at least 80%, at least 85%) to an amino acid sequence of SEQ ID NO:8**; b) a conservative variant of the amino acid sequence of SEQ ID NO:8; c) the amino acid sequence of SEQ ID NO:8, **wherein the polypeptide has RFX4_v3 activity**, and fourteen consecutive amino acids within the N-terminus of the polypeptide are at least 90% identical to residues 1-14 of SEQ ID NO:8; a vector and an *in vitro* host cell comprising the same isolated nucleic acid molecule; as well as a method for producing the same encoded variant RFX_v3 polypeptide.

Apart from the disclosure of full-length novel brain specific variant transcripts of RFX4 having SEQ ID NO:37 (human RFX4_v3), SEQ ID NO:38 (mouse SEQ ID NO:39) and SEQ ID NO:39 (zebra), in which both mouse and human RFX4_v3 transcripts encode identical the first 14 N-terminal amino acid residues while the zebra RFX4_v3 transcript encodes for a similar N terminal amino acid sequence with the substitution of a His by a Leu at residue number 2; the instant specification **fails to describe the essential core structure(s) or element(s) possessed by other isolated nucleic acid molecules as broadly claimed such that the encoded polypeptide has RFX4_v3 activity which is defined as any activity that promotes the development of the brain's ventricular system, the absence of which activity is demonstrated by the development of hydrocephalus, as well as the ability to bind to RFX4_v3 specific antibodies (see instant specification on page 11, lines 3-5 and claim 69)**. What exactly is the core structure(s) or element(s) that is responsible for the RFX4_v3 activity

that an isolated nucleic acid molecule having at least 70% or 90% identical to SEQ ID NO:37, or a nucleic acid molecule encoding a polypeptide comprising **an amino acid sequence at least 70% identical to any amino acid sequence as set forth in SEQ ID NO:8 (not necessarily the entire SEQ ID NO:8)** as long as fourteen consecutive amino acids within its N-terminus are at least 90% identical to residues 1-14 of SEQ ID NO:8 should possess or to be produced in the claimed method? The instant specification merely showed that the development of a graded hydrocephalus in a transgenic mouse is the result of a partial and complete deficiency of its full-length RFX4_v3 transcripts. Furthermore, **there is no evidence of record or in the prior art at the effective filing date of the present application that the N-terminal sequence containing the first 14 amino acid residues of SEQ ID NO:8 is responsible for any activity associated with the development of the brain's ventricular system, let alone for 14 consecutive amino acids within the N-terminus of a polypeptide are at least 90% identical to residues 1-14 of SEQ ID NO:8 as broadly claimed**. Moreover, at about the effective filing date of the present application (4/19/02) the physiological functions of RFX gene products, including alternatively spliced variants of RFX4 such as RFX4_v1 and RFX4_v2, were unknown as evidenced at least by the teachings of Morotomi-Yano et al. (J. Biol. Chem. 277:836-842, 2002; IDS), Blackshear et al. (Development 130:4539-4552, 2003; IDS) and Araki et al. (J. Biol. Chem. 279:10237-10242, 2004). Furthermore, at about the effective filing date of the present application Old et al (US 2003/0180298 A1) also disclosed the nucleic acid sequence for RFX4-E whose N-terminal region comprises identical 1-13 residues of SEQ ID NO:8,

and yet it is clearly a distinct molecule from RFX4_v3 or RFX4-D, and of course without any RFX4_v3 activity (see at least Fig. 7 and SEQ ID NOs 67-69). Then, once again the issue is which essential characteristic(s) or element(s) possessed by the isolated nucleic acid molecule to endow the ability to bind to RFX4_v3 specific antibodies and not by other antibodies? The instant specification also fails to provide **a representative number of species for a broad genus of an isolated nucleic acid molecule encoding a polypeptide having RFX4 v3 activity as broadly claimed or a representative number of species for the same broad genus of encoded variant RFX v3 polypeptide having RFX4 v3 activity to be produced in a method as broadly claimed.**

Furthermore, please note that it is well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar and identical biological activities. For example, it is well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000);

Kyrpides et al. (Mol. Microbiology 32:886-887, 1999); Wells et al. (J. Leukocyte Biology 61:545-550, 1997); and Gerhold et al. (BioEssays 18:973-981, 1996).

The claimed invention as a whole is not adequately described **if the claims require essential or critical elements that are not adequately described in the specification.** Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). A skilled artisan cannot fully envision the detailed structure of any essential core structure(s) or element(s) for a representative number of species for a broad genus of an isolated nucleic acid molecule encoding a polypeptide having RFX4_v3 activity as broadly claimed, a vector and a host cell comprising the same or the same encoded variant RFX_v3 polypeptide having RFX4_v3 activity to be produced in a method as broadly claimed. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 4/24/08 (pages 12-15) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

1. Applicants argue that the specification provides a sufficient description of a representative number of species in the genus of nucleic acid sequences encoding RFX4_v3 polypeptides having RFX4_v3 activity, for examples nucleic acid encoding human, murine and zebrafish RFX4_v3 polypeptides. In addition, the specification clearly describes nucleic acid sequences encoding RFX4_v3 polypeptide variants having, for example 70%, 80%, 90% and 95% sequence identity with SEQ ID NO:8 as well as conservative variants of SEQ ID NO:8; and the specification clearly describes that the variant will "function in a fashion similar to the wild type protein".

First, it should be noted that the clams are not limited to full-length novel brain specific variant transcripts of RFX4 having SEQ ID NO:37 (human RFX4_v3), SEQ ID NO:38 (mouse SEQ ID NO:39) and SEQ ID NO:39 (zebra). With respect to the elected species of SEQ ID NO:37, the claims encompass an isolated nucleic acid molecule encoding a RFX4_v3 polypeptide, wherein the polypeptide comprises any amino acid sequence at least 70% identical to any amino acid sequence set forth as SEQ ID NO:8 (not necessarily limited to the full length amino acid sequence of SEQ ID NO:8) as long as the polypeptide has RFX4_v3 activity and fourteen consecutive amino acids within

the N-terminus of the polypeptide are at least 90% identical to residues 1-14 of SEQ ID NO:8.

Second, as already noted in the above rejection there is no direct relationship between any particular sequence(s) with any of the RFX4_v3 activity. For example, What exactly is the core structure(s) or element(s) that is responsible for the RFX4_v3 activity that an isolated nucleic acid molecule having at least 70% or 90% identical to SEQ ID NO:37, or a nucleic acid molecule encoding a polypeptide comprising **an amino acid sequence at least 70% identical to any amino acid sequence as set forth in SEQ ID NO:8 (not necessarily the entire SEQ ID NO:8)** as long as fourteen consecutive amino acids within its N-terminus are at least 90% identical to residues 1-14 of SEQ ID NO:8 should possess or to be produced in the claimed method? **There is no evidence of record or in the prior art at the effective filing date of the present application that the N-terminal sequence containing the first 14 amino acid residues of SEQ ID NO:8 is responsible for any activity associated with the development of the brain's ventricular system, let alone for 14 consecutive amino acids within the N-terminus of a polypeptide are at least 90% identical to residues 1-14 of SEQ ID NO:8 as broadly claimed**. Additionally, at about the effective filing date of the present application Old et al (US 2003/0180298 A1) also disclosed the nucleic acid sequence for RFX4-E whose N-terminal region comprises identical 1-13 residues of SEQ ID NO:8, and yet it is clearly a distinct molecule from RFX4_v3 or RFX4-D (see at least Fig. 7 and SEQ ID NOs 67-69). Then, the issue is which essential characteristic(s) or element(s) possessed by the isolated nucleic acid molecule to

endow the ability to bind to RFX4_v3 specific antibodies and not by other antibodies? Furthermore, the physiological functions of RFX gene products, including alternatively spliced variants of RFX4 such as RFX4_v1 and RFX4_v2, were also unknown as evidenced at least by the teachings of Morotomi-Yano et al. (J. Biol. Chem. 277:836-842, 2002; IDS), Blackshear et al. (Development 130:4539-4552, 2003; IDS) and Araki et al. (J. Biol. Chem. 279:10237-10242, 2004).

Third, the simple description or assertion that a variant will "function in a fashion similar to the wild type protein" is not sufficient for overcoming the lack of written description for the broadly claimed invention for the reasons discussed above.

2. Applicants also argue that the specification discloses a number of relevant identifying characteristics of the RFX4_v3 polypeptides encoded by the claimed nucleic acid sequences that would enable one of skill in the art to readily identify members of this genus, even if they were not specifically described in the specification. For example, the RFX4_v3 polypeptides "belong to the winged-helix subfamily of helix-turn-helix transcription factors, and are so named because they bind to 'X-boxes'"; RFX members are evolutionarily conserved transcription factors that share a highly conserved winged helix DNA-binding domain, dimerization domain and B and C boxes; and that the RFX4_v3 polypeptides are defined by a unique set of amino terminal 14 amino acids.

First, please note that at least RFX4 spliced variants such as **RFX4 v1 and RFX4 v2 share one or more of the above mentioned domains and yet none of them has any RFX4 v3 activity**.

Second, once again with respect to the elected SEQ ID NO:37 the claims are not necessarily limited to an encoded polypeptide comprising residues 1-14 of SEQ ID NO:8. Moreover, **there is no evidence of record or in the prior art at the effective filing date of the present application that the N-terminal sequence containing the first 14 amino acid residues of SEQ ID NO:8 is responsible for any activity associated with the development of the brain's ventricular system, let alone for 14 consecutive amino acids within the N-terminus of a polypeptide are at least 90% identical to residues 1-14 of SEQ ID NO:8 as broadly claimed**.

3. Applicants further argue that there is no requirement that all encompassed species to be specifically identified in the specification because the specification provides a sufficient description of representative number of species and a number of relevant, identifying characteristics that sufficiently describe the genus of nucleic acid sequences encoding RFX4_v3 polypeptides. Additionally, based on the known conserved domains of the claimed sequences, it was well known to those of skill in the art at the time the application was filed which residues can not be substituted.

Please refer to the examiner's responses in the preceding paragraphs why the instant specification fails to provide a sufficient description of representative number of species and a number of relevant, identifying characteristics that sufficiently describe

the genus of nucleic acid sequences encoding RFX4 v3 polypeptides having RFX4 v3 activity as broadly claimed. Since there is no direct relationship or association between any particular conserved domain(s) or specific combinations of domains with any RFX4_v3 activity, those of skill in the art at the time the application was filed would not know which residues in which domain(s) to be substituted and/or deleted and/or inserted so that the RFX4_v3 activity would still be retained for an encoded polypeptide as broadly claimed.

Accordingly, claims 5-6, 8-13, 25 and 65-71 are rejected under 35 U.S.C. 112, first paragraph, for the lack of Written Description for the reasons discussed above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Amended claims 15-17, 19-21, 26-27 and new claims 72-73 are rejected under 35 U.S.C. 102(e) as being anticipated by Venter et al. (US 6,812,339; IDS). ***This is a modified rejection necessitated by Applicant's amendment.***

With respect to the elected species, Venter et al disclosed genomic nucleotide sequences, transcript sequences including SEQ ID NO:416, encoded amino acid

sequences that contain single nucleotide polymorphisms (see at least Summary of the Invention; col. 5, line 60 continues to line 25 of col.6; col. 9, line 53 continues to line 62). The nucleotide sequence of SEQ ID NO:416 is 72.3% identical (with 99.3% best local similarity) to the nucleotide sequence of SEQ ID NO:37 of the present invention (see attached sequence searches). Such a nucleotide sequence would hybridize to a polynucleotide consisting of nucleotides 1-42 of SEQ ID NO: 37 or a polynucleotide comprising at least 20 contiguous nucleotides in the region between nucleotides 1 and 42 of SEQ ID NO: 37 under low stringency and/or high stringency, particularly with a probe of 42 nucleotides or 20 nucleotides in length, **because it has the sequence of 7 identical consecutive nucleotides TTCCACA (100%) at its 5' end as nucleotides 36-42 of the polynucleotide**. Furthermore, please also note that the term "RFX4_v3 polypeptide" is defined by the instant specification to include fragments of the RFX4_v3 sequence as well as other domains within the full-length RFX_v3 polypeptide (see at least page 10, lines 28-34 of the instant specification). Venter et al further teach that the disclosed nucleic acid molecules may be double stranded molecules and include both a protein encoding strand (sense strand) as well as a complementary nucleotide sequence comprising a sequence complementary to the protein encoding strand or anti-sense strand (col. 8, lines 1-51). The isolated nucleic acid molecule can be cloned into an expression vector, introduced into a host cell such as a bacterial cell, a yeast cell or a mammalian cell for purifying the encoded variant protein (col. 11, lines 40-50; col. 19, lien 39 continues to line 6 of col. 23).

The teachings of Venter et al meet all the limitation of the instant claims as broadly written. Accordingly, the reference anticipates the instant claims.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 4/24/08 (pages 15-16) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicants argue basically that since SEQ ID NO:416 of Venter et al aligns with SEQ ID NO:37 beginning at residue 36 of SEQ ID NO:37, SEQ ID NO:416 does not hybridize to a polynucleotide consisting of residues 1-42 of SEQ ID NO:37 as required in claim 15. Therefore, the reference does not anticipate the instant claims.

First, it should be noted that it is not necessarily that the isolated nucleic acid molecule of either independent claim 15 or independent claim 72 contains nucleotides 1-42 of SEQ ID NO:37.

Second, as already noted in the above rejection SEQ ID NO:416 of Venter et al would hybridize to a polynucleotide consisting of nucleotides 1-42 of SEQ ID NO: 37 or a polynucleotide comprising at least 20 contiguous nucleotides in the region between nucleotides 1 and 42 of SEQ ID NO: 37 under low stringency and/or high stringency, particularly with a probe of 42 nucleotides or 20 nucleotides in length, **because it has the sequence of 7 identical consecutive nucleotides TTCCACA (100%) at its 5' end as nucleotides 36-42 of the polynucleotide**.

The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Old et al (US 2003/0180298 A1) disclosed nucleic acid sequences for RFX4-D and RFX4E, with the coding sequence for RFX4-D exhibits 99.7% similarity to SEQ ID NO:37 of the present invention (see at least Fig. 7 and SEQ ID NOs. 65 and 66). However, this reference is not a prior art because these RFX4-D and RFX4E nucleic acid sequences were not disclosed in any of its priority documents prior to October 01, 2002.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN/
Primary Examiner, Art Unit 1633